



Docket No. 826.1335C/WFH

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of:

Kensaku IMAI; et al.

Serial No.: 09/785,269

Group Art Unit: 1631

Confirmation No. 2896

Filed: February 20, 2001

Examiner:

For: **METHOD AND APPARATUS FOR AUTOMATICALLY REMOVING VECTOR UNIT IN  
DNA BASE SEQUENCE**

**SECOND PRELIMINARY AMENDMENT**

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

Before examination of the above-identified application, please amend the application as follows:

**I. AMENDMENTS**

**A. In the Claims (37 C.F.R. §1.121(c)(1)(i))**

Please **CANCEL** claim 49.

Claims 45-48 and 50-63 have been re-numbered and amended as follows:

23. (AS ONCE AMENDED) A method for manipulating base sequence data of a vector, comprising:

storing data identifying each of restriction enzymes and data of base sequences at a plurality of restriction enzyme sites of a plurality of vectors correspondingly, in a database;

searching base sequence data of a recombinant DNA obtained by splicing an object DNA fragment into a vector;

obtaining the base sequence data at a front restriction enzyme site and the base sequence data at a back restriction enzyme site, as specified by corresponding to a restriction enzyme used for cleaving the vector and a restriction enzyme used for obtaining the object DNA fragment, from the database;

generating a first forward retrieval key using the obtained base sequence data of the front restriction enzyme site and a first backward retrieval key using the obtained base sequence data of the back restriction enzyme site;

retrieving base sequence data of the recombinant DNA obtained by a search using the first forward and first backward retrieval keys, and specifying a junction between the vector and the object DNA fragment; and

removing nucleic acid molecules of the vector at the specified junction.

24. (AS ONCE AMENDED) The method according to Claim 23,

wherein sequence data of the first forward retrieval key and of the first backward retrieval key are generated by base sequence data of the vector entered in a vector database, data of a multiple cloning site in the vector, and data of a restriction enzyme site in the multiple cloning site,

wherein data of a forward base sequence from a cleaving point in the restriction enzyme site in the multiple cloning site of the vector are acquired from the database, and a second forward retrieval key is generated using the acquired forward base sequence data of the cleaving point of the restriction enzyme site of the vector,

performing first homology retrieval on condition that a first similarity value between retrieval base sequence data of the recombinant DNA and the first forward and first

backward retrieval keys is equal to or larger than a predetermined value, obtaining a candidate for a base sequence at the junction between the vector and the object DNA fragment according to a result of the first homology retrieval, and performing a second homology retrieval on condition that a second similarity value between base sequence data of a plurality of first candidates for the junction, and base sequence data of the second forward retrieval key, is equal to or larger than a predetermined value.

25. (AS ONCE AMENDED) The method according to Claim 23,

wherein the sequence data of the first forward retrieval key and of the first backward retrieval key are generated by base sequence data of the vector entered in a vector database, data of a multiple cloning site in the vector, and data of a restriction enzyme site in the multiple cloning site,

wherein forward base sequence data of a forward cleaving point of the restriction enzyme site of the vector, and backward base sequence data of a backward cleaving point of the vector are acquired from the database, and a second forward retrieval key and a second backward retrieval key are generated using the base sequence data of the acquired forward and backward base sequence data of the cleaving points, respectively,

performing a first homology retrieval on condition that a first similarity value between retrieval base sequence data of the recombinant DNA and the first forward and first backward retrieval keys is equal to or larger than a predetermined value,

obtaining a candidate for a base sequence at the junction between the vector and the object DNA fragment according to a result of the first homology retrieval, and

performing a second homology retrieval on condition that a second similarity value between base sequence data of a plurality of first candidates for the junction, and base sequence data of the second forward retrieval key, is equal to or larger than a predetermined value.

26. (AS ONCE AMENDED) The method according to Claim 25, wherein the sequence data of the first forward and first backward retrieval keys are generated by base sequence data of the vector entered in a vector database, data of a multiple cloning site in the vector, and data of a restriction enzyme site in the multiple cloning site, and

wherein the second homology retrieval is performed using both the second forward and second backward retrieval keys.

28. (AS ONCE AMENDED) The method according to Claim 23,

wherein backward base sequence data from a cleaving point in a multiple cloning site of the vector corresponding to the restriction enzyme are acquired from the database, and a second backward retrieval key is generated using the acquired backward base sequence data of the cleaving point, and

performing a first homology retrieval on condition that a first similarity value between retrieval base sequence data of the recombinant DNA and the first forward and first backward retrieval keys is equal to or larger than a predetermined value;

obtaining a candidate for a base sequence at a junction between the vector and the object DNA fragment according to a result of the first homology retrieval; and

performing a second homology retrieval on condition that a second

similarity value between base sequence data of a first candidate for the junction, screened by using the first retrieval keys, and base sequence data of the second backward retrieval key is equal to or larger than a predetermined value.

29. (AS ONCE AMENDED) The method according to Claim 28,

wherein said nucleic acid molecules of said vector are removed from the recombinant DNA sequence data, when the area specified by the second homology retrieval is one.

30. (AS ONCE AMENDED) The method according to Claim 25, further comprising:

obtaining, as a forward vector unit candidate for the vector base sequence, a forward base sequence selected by the second homology retrieval, and a base sequence before said forward base sequence; and

obtaining, as a backward vector unit candidate for the vector base sequence, a backward base sequence selected by the second homology retrieval, and a base sequence after said backward base sequence.

31. (AS ONCE AMENDED) The method according to Claim 29,

wherein said forward vector unit candidate and said backward vector unit candidate are removed from the recombinant DNA sequence data, when there is only one candidate respectively for the specified forward and backward vector units, and the specified forward and backward vector units do not overlap each other.

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32. (AS ONCE AMENDED) A device for removing nucleic acid molecules of a vector from a recombinant DNA base sequence, obtained as a result of performing a cloning process by integrating an object DNA fragment into a vector, comprising:

    a database storing data identifying each of restriction enzymes, and data of base sequences at a plurality of restriction enzyme sites of a plurality of vectors correspondingly;

    an obtaining unit obtaining base sequence data at a front restriction enzyme site and base sequence data at a back restriction enzyme site, as specified corresponding to a restriction enzyme used for cleaving the vector and a restriction enzyme used for obtaining the object DNA fragment, from the database;

    a generation unit generating a first forward retrieval key using the obtained base sequence data of the front restriction enzyme site, and a first backward retrieval key using the obtained base sequence data of the back restriction enzyme site; and

    a retrieving unit retrieving base sequence data of the recombinant DNA obtained using the first forward and first backward retrieval keys, and specifying a junction between the vector and the object DNA fragment.

33. (AS ONCE AMENDED) The device according to Claim 32, further comprising:

    display means,

    wherein said vector is included in a vector list displayed on said display means, and

    wherein at least one of said specified restriction enzymes is included in a restriction enzyme list displayed on said display means.

34. (AS ONCE AMENDED) The device according to Claim 32, further comprising:

program storage means for storing at least one of:

a program for generating the retrieval keys by controlling said generation unit;

a program for specifying the vector base sequence by controlling said retrieving unit; and

a program for removing the vector base sequence.

35. (AS ONCE AMENDED) The device according to Claim 32,

wherein said retrieving unit specifies using the first retrieval key as a junction between the vector base sequence data and the object DNA fragment sequence data.

36. (AS ONCE AMENDED) The device according to Claim 35,

wherein said retrieving unit specifies, as the junction, a portion in the DNA base sequence data in which a number of bases matching a base sequence of the first retrieval key is equal to or larger than a predetermined value.

37. (AS ONCE AMENDED) The device according to Claim 32,

wherein said retrieving unit specifies using, as the first retrieval key, a first junction and a second junction between the vector base sequence and the object DNA fragment.

38. (AS ONCE AMENDED) The device according to Claim 32,

wherein each of said first forward and first backward retrieval keys

includes sequence data including an end portion of the object DNA fragment and sequence data including an end portion of the vector base sequence, and specifies a candidate for the junction between the vector base sequence and the object DNA fragment.

39. (AS ONCE AMENDED) The device according to Claim 38,  
wherein a second retrieval key, including sequence data longer than that  
of said first forward and first backward retrieval keys, is generated, and the junction is specified  
using the second retrieval key.

40. (AS ONCE AMENDED) The device according to Claim 39,  
wherein said object DNA fragment is specified by removing the junction  
and sequence data distal to the junction and the object DNA fragment from the DNA base  
sequence.

41. (AS ONCE AMENDED) A computer-readable storage medium on which is  
recorded a program enabling a computer to execute an operation process of a base sequence  
of a recombinant DNA obtained by integrating an object DNA into a vector, said process  
comprising the steps of:

storing data identifying each of restriction enzymes and data of base  
sequences at a plurality of restriction enzyme sites of a plurality of vectors correspondingly, in a  
database;

obtaining base sequence data at a front restriction enzyme site and base  
sequence data at a back restriction enzyme site, as specified corresponding to a restriction

enzyme used for cleaving the vector and a restriction enzyme used for obtaining the object DNA fragment, from the database;

generating a forward retrieval key based on the obtained base sequence data of the front restriction enzyme site, and a backward retrieval key using the obtained base sequence data of the back restriction enzyme site;

retrieving base sequence data of the recombinant DNA obtained by a search using the forward and backward retrieval keys, and

specifying a junction between the vector and the object DNA fragment for removing nucleic acid molecules of the vector.

Attached hereto is a "Version With Markings to Show Changes Made," comprising marked-up version of the changes made to the claims.

## II. REMARKS

This Second Preliminary Amendment is submitted to improve the form of the claims, as pending, and to address various 35 U.S.C. §112 issues raised during the parent's prosecution.

More particularly claim 49 has been canceled. In addition, the new claims 45-63 added by way of the February 20, 2001 Preliminary Amendment had been erroneously numbered. The numbering has been corrected herein for the remaining pending claims 45-48 and 50-63, i.e., to 23-26 and 28-41. The undersigned apologizes for any inconvenience to the Office.

Further, the August 18, 2000 Final Office Action in the parent raised various 35 U.S.C. §112, 2nd paragraph issues, which are believed addressed by the amendments herein.

III. CONCLUSION

In light of the above amendments and remarks, it is respectfully submitted that the claims 23-26 and 28-41 are now in condition for allowance.

If there are any formal matters remaining after this response, the undersigned would appreciate a telephone conference with the Examiner to attend to these matters.

If any further fees are required in connection with the filing of this Preliminary Amendment, please charge same to our Deposit Account No. 19-3935.

Respectfully submitted,  
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**ATTACHMENT**

VERSION WITH MARKINGS TO SHOW CHANGES MADE - 37 C.F.R. '121(c)(1)(ii)

[45.]23. (ONCE AMENDED) A method for manipulating base sequence data of a vector, comprising:

storing data identifying each of [a] restriction enzymes and data of [a] base sequences at a plurality of [a] restriction enzyme sites of a plurality of vectors correspondingly, in a database;

searching [for] base sequence data of a recombinant DNA obtained by [integrating] splicing an object DNA fragment into a vector;

obtaining the base sequence data [of] at a front restriction enzyme site and the base sequence data [of] at a back restriction enzyme site, as specified by corresponding to a restriction enzyme used for cleaving the vector and a restriction enzyme used for obtaining the object DNA fragment, from the database;

generating a first forward retrieval key [based on] using the obtained base sequence data of the front restriction enzyme site and a first backward retrieval key [based on] using the obtained base sequence data of the back restriction enzyme site;

retrieving base sequence data of the recombinant DNA obtained by [the] a search [based on] using the first forward and first backward retrieval keys, and specifying a junction between the vector and the object DNA fragment; and

removing nucleic acid molecules of the vector at the specified junction.

[46.]24. (ONCE AMENDED) The method according to Claim [45] 23,

wherein sequence data of the first forward retrieval key and of the first backward retrieval key are generated by base sequence data of the vector entered in a vector database, data of a multiple cloning site in the vector, and data of a restriction enzyme site in the multiple cloning site,

wherein[, if the restriction enzyme used to cleave the vector and the restriction enzyme used to obtain the object DNA fragment are designated,] data of a forward base sequence from a cleaving point in the restriction enzyme site in the multiple cloning site of the vector are acquired from the database, and a second forward retrieval key is generated [based on] using the acquired forward base sequence data of the cleaving point of the restriction enzyme site of the vector,

performing first homology retrieval on condition that a first similarity value between [the] retrieval base sequence data of the recombinant DNA and the first forward and first backward retrieval keys is equal to or larger than a predetermined value,

obtaining a candidate for a base sequence at [a] the junction between the vector and the object DNA fragment according to a result of the first homology retrieval, and

performing a second homology retrieval on condition that a second similarity value between base sequence data of a plurality of first candidates for the junction,[ screened by using the first retrieval keys,] and base sequence data of the second forward retrieval key, is equal to or larger than a predetermined value.

[47.]25. (ONCE AMENDED) The method according to Claim [45] 23,

wherein the sequence data of the first forward retrieval key and of the first backward retrieval key are generated by base sequence data of the vector entered in a vector database, data of a multiple cloning site in the vector, and data of a restriction enzyme site in the multiple cloning site,

wherein[, if the restriction enzyme used to cleave the vector and the restriction enzyme used to obtain the object DNA fragment are designated,] forward base sequence data of a forward cleaving point of the restriction enzyme site of the vector, and backward base sequence data of a backward cleaving point of the vector are acquired from the database, and a second forward retrieval key and a second backward retrieval key are generated [based on] using the base sequence data of the acquired forward and backward base sequence data of the cleaving points, respectively,

performing a first homology retrieval on condition that a first similarity value between [the] retrieval base sequence data of the recombinant DNA and the first forward and first backward retrieval keys [are] is equal to or larger than a predetermined value,

obtaining a candidate for a base sequence at [a] the junction between the vector and the object DNA fragment according to a result of the first homology retrieval, and

performing a second homology retrieval on condition that a second similarity value between base sequence data of a plurality of first candidates for the junction, [screened by using the first retrieval keys,] and base sequence data of the second forward retrieval key, is equal to or larger than a predetermined value.

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[48.]26. (ONCE AMENDED) The method according to Claim [47] 25, wherein the sequence data of the first forward and first backward retrieval keys are generated by base sequence data of the vector entered in a vector database, data of a multiple cloning site in the vector, and data of a restriction enzyme [size] site in the multiple cloning site, and wherein the second homology retrieval is performed using both the second forward and second backward retrieval keys.

[50.]28. (ONCE AMENDED) The method according to Claim [45] 23, wherein[, if the restriction enzyme used to cleave the vector and a restriction enzyme used to obtain the object DNA fragment are designated,] backward base sequence data from a cleaving point in a multiple cloning site of the vector corresponding to the [designated] restriction enzyme are acquired from the database, and a second backward retrieval key is generated [based on] using the acquired backward base sequence data of the cleaving point, and

performing a first homology retrieval on condition that a first similarity value between [the] retrieval base sequence data of the recombinant DNA and the first forward and first backward retrieval keys [are] is equal to or larger than a predetermined value;

obtaining a candidate for a base sequence at a junction between the vector and the object DNA fragment according to a result of the first homology retrieval; and

performing a second homology retrieval on condition that a second similarity value between base sequence data of a first candidate for the junction, screened by using the first retrieval keys, and base sequence data of the second backward retrieval key is equal to or larger than a predetermined value.

[51.]29. (ONCE AMENDED) The method according to Claim [50] 28, wherein said nucleic acid molecules of said vector [is] are removed from the recombinant DNA sequence data, when the area specified by the second homology retrieval is one.

[52.]30. (ONCE AMENDED) The method according to Claim [47] 25, further comprising:

obtaining, as a forward vector unit candidate for the vector base sequence, a forward base sequence [specified as a result of] selected by the second homology retrieval, and a base sequence before said forward base sequence; and

obtaining, as a backward vector unit candidate for the vector base sequence, a backward base sequence [specified as a result of] selected by the second homology retrieval, and a base sequence after said backward base sequence.

[53.]31. (ONCE AMENDED) The method according to Claim [51] 29, wherein said forward vector unit candidate and said backward vector unit candidate are removed from the recombinant DNA sequence data, when there is only one candidate respectively for the specified forward and backward vector units, and the specified forward and backward vector units do not overlap each other.

[54.]32. (ONCE AMENDED) A device for removing nucleic acid molecules of a vector from a recombinant DNA base sequence, obtained as a result of performing a cloning process by integrating an object DNA fragment into a vector, comprising:

a database storing data identifying each of [a] restriction enzymes, and data of base sequences at a plurality of [a] restriction enzyme sites of a plurality of vectors correspondingly;

an obtaining unit obtaining base sequence data [of] at a front restriction enzyme site and base sequence data [of] at a back restriction enzyme site, as specified [by the] corresponding to a restriction enzyme used for cleaving the vector and [the] a restriction enzyme used for obtaining the object DNA fragment, from the database;

a generation unit generating a first forward retrieval key [based on] using the obtained base sequence data of the front restriction enzyme site [of a vector], and a first backward retrieval key [based on] using the obtained base sequence data of the back restriction enzyme site; and

a retrieving unit retrieving base sequence data of the recombinant DNA obtained [based on] using the first forward and first backward retrieval keys, and specifying a junction between the vector and the object DNA fragment [based on the retrieval result].

[55.]33. (ONCE AMENDED) The device according to Claim [54] 32, further comprising:

display means,

wherein said vector is included in a vector list displayed on said display means, and

wherein at least one of said specified restriction enzymes is included in a restriction enzyme list displayed on said display means.

[56.]34. (ONCE AMENDED) The device according to Claim [54] 32, further comprising:

program storage means for storing at least one of:

a program for generating the retrieval keys by controlling said generation unit;

a program for specifying the vector base sequence by controlling said retrieving unit; and

a program for removing the vector base sequence.

[57.]35. (ONCE AMENDED) The device according to Claim [54] 32, wherein said retrieving unit specifies using the first retrieval key as a junction between the vector base sequence data and the object DNA fragment sequence data.

[58.]36. (ONCE AMENDED) The device according to Claim [57] 35, wherein said retrieving unit specifies, as the junction, a portion in the DNA base sequence data in which a number of bases matching a base sequence of the first retrieval key is equal to or larger than a predetermined value.

[59.]37. (ONCE AMENDED) The device according to Claim [54] 32, wherein said retrieving unit specifies using, as the first retrieval key, a first junction and a second junction between the vector base sequence and the object DNA fragment.

[60.]38. (ONCE AMENDED) The device according to Claim [54] 32, wherein each of said [retrieval key is] first forward and first backward

retrieval keys [including] includes sequence data including an end portion of the object DNA fragment and sequence data including an end portion of the vector base sequence, and specifies a candidate for [a] the junction between the vector base sequence and the object DNA fragment.

[61.]39. (ONCE AMENDED) The device according to Claim [60] 38,

wherein a second retrieval key, including sequence data longer than that of said first forward and first backward retrieval keys, is generated, and the junction is specified using the second retrieval key.

[62.]40. (ONCE AMENDED) The device according to Claim [61] 39,

wherein said object DNA fragment is specified by removing the junction and sequence data distal to the junction and the object DNA fragment from the DNA base sequence.

[63.]41. (ONCE AMENDED) A computer-readable storage medium on which is recorded a program enabling a computer to execute an operation process of a base sequence of a recombinant DNA obtained by integrating an object DNA into a vector, said process comprising the steps of:

storing data identifying each of [a] restriction enzymes and data of [a] base sequences at a plurality of [a] restriction enzyme sites of a plurality of vectors correspondingly, in a database;

obtaining base sequence data[, of] at a front restriction enzyme site and base sequence data [of] at a back restriction enzyme site, as specified [by the] corresponding to

a restriction enzyme used for cleaving the vector and [the] a restriction enzyme used for obtaining the object DNA fragment, from the database;

generating a forward retrieval key based on the obtained base sequence data of the front restriction enzyme site, and a backward retrieval key [based on] using the obtained base sequence data of the back restriction enzyme site;

retrieving base sequence data of the recombinant DNA obtained by a search [based on] using the forward and backward retrieval keys, and

specifying a junction between the vector and the object DNA fragment for removing [the] nucleic acid molecules of the vector.